

## Quantitation of Antibiotics in Exhaled breath: a pilot study (ANTIBEX-trial)

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### Introduction

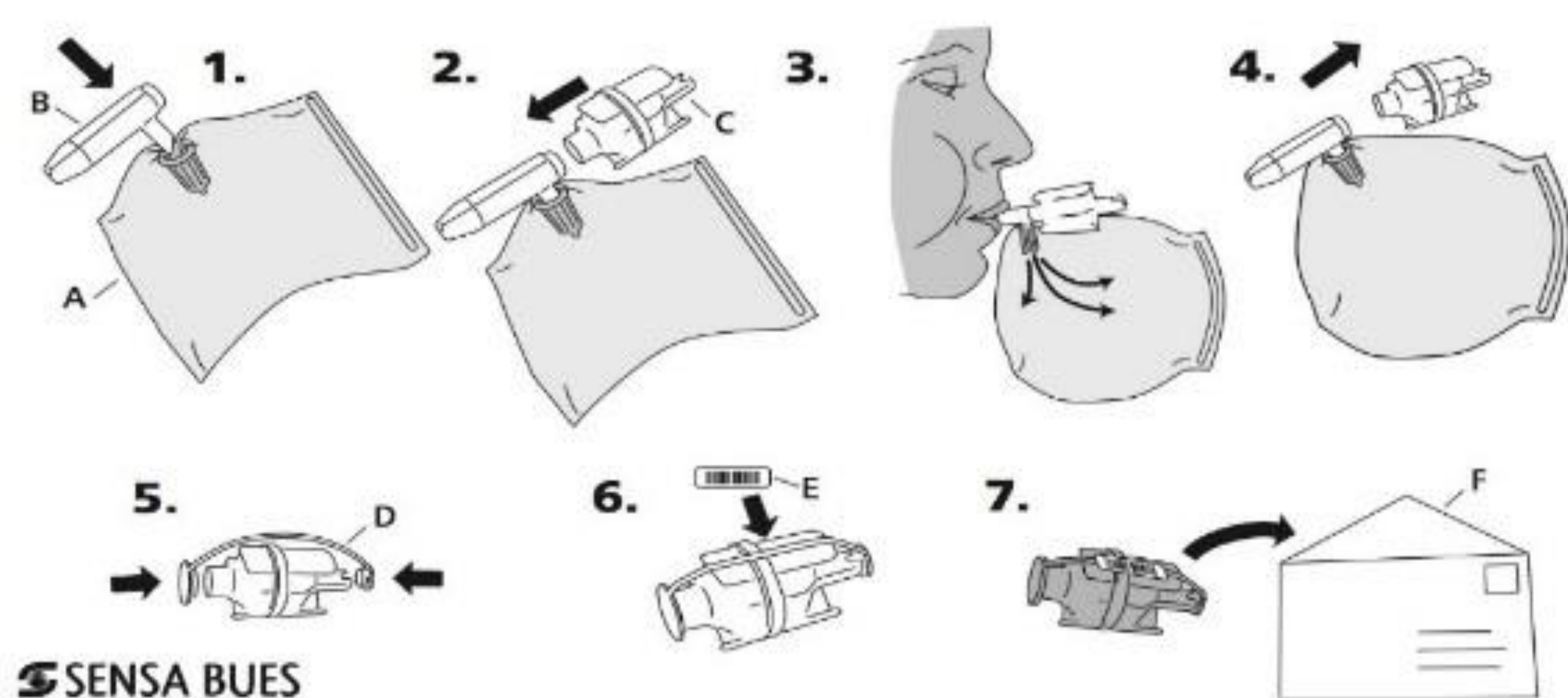
Infections are a frequent and possibly life-threatening problem in intensive care unit patients, and antibiotic therapy is one of the cornerstones of the treatment.

Therapeutic drug monitoring has been proposed to optimise antibiotic therapy but measuring tissue concentrations remains difficult (1).

The ExaBreath® device (SensAbues AB, Sollentuna, Sweden, Fig. 1) has proven reliable for collecting exhaled breath to detect recreational drugs but has not been evaluated for measuring antibiotic concentrations (2,3).

#### AIMS:

To explore the feasibility and safety of the ExaBreath®-device to determine antibiotic concentrations in exhaled air.



Use of the ExaBreath®-device (image downloaded from [www.sensabues.com](http://www.sensabues.com))

Figure 1. The sampling method with the ExaBreath® device

### Results

Nine patients (7 men, 2 women) were treated with piperacillin/tazobactam, 2 (men) with meropenem.

Seven out of 11 patients were able to exhale in a standardized way in the device. The remaining 4 did not exhale correctly, became tired or the control container filled too slowly.

No complications directly related to the procedure occurred.

Antibiotic concentrations were detectable in exhaled breath. Measured concentration were between 5.54pg and 1253pg/filter.

No correlation between the piperacillin concentration in the exhaled breath and plasma was found.

A positive correlation between piperacillin concentration in exhaled breath and breath condensate was found.

### Methods

Eleven spontaneously breathing patients treated with piperacillin/tazobactam or meropenem and considered capable of exhaling for 3 minutes through the ExaBreath®-device participated.

Patients exhaled through the device until the control container was full (which equates to 30L of exhaled breath), or until the patient wanted to stop.

Samples were analyzed using liquid chromatography high resolution mass spectrometry. The devices were opened and the filters were extracted with 2 mL 70:30 4% NaCl in water:isopropanol containing piperacillin-D<sub>5</sub> and meropenem-D<sub>6</sub> as internal standards. A 3D printed spacer was used for centrifugation (Fig. 2) The analysis was performed by liquid chromatography high-resolution mass spectrometry on a Thermo Q-Exactive.

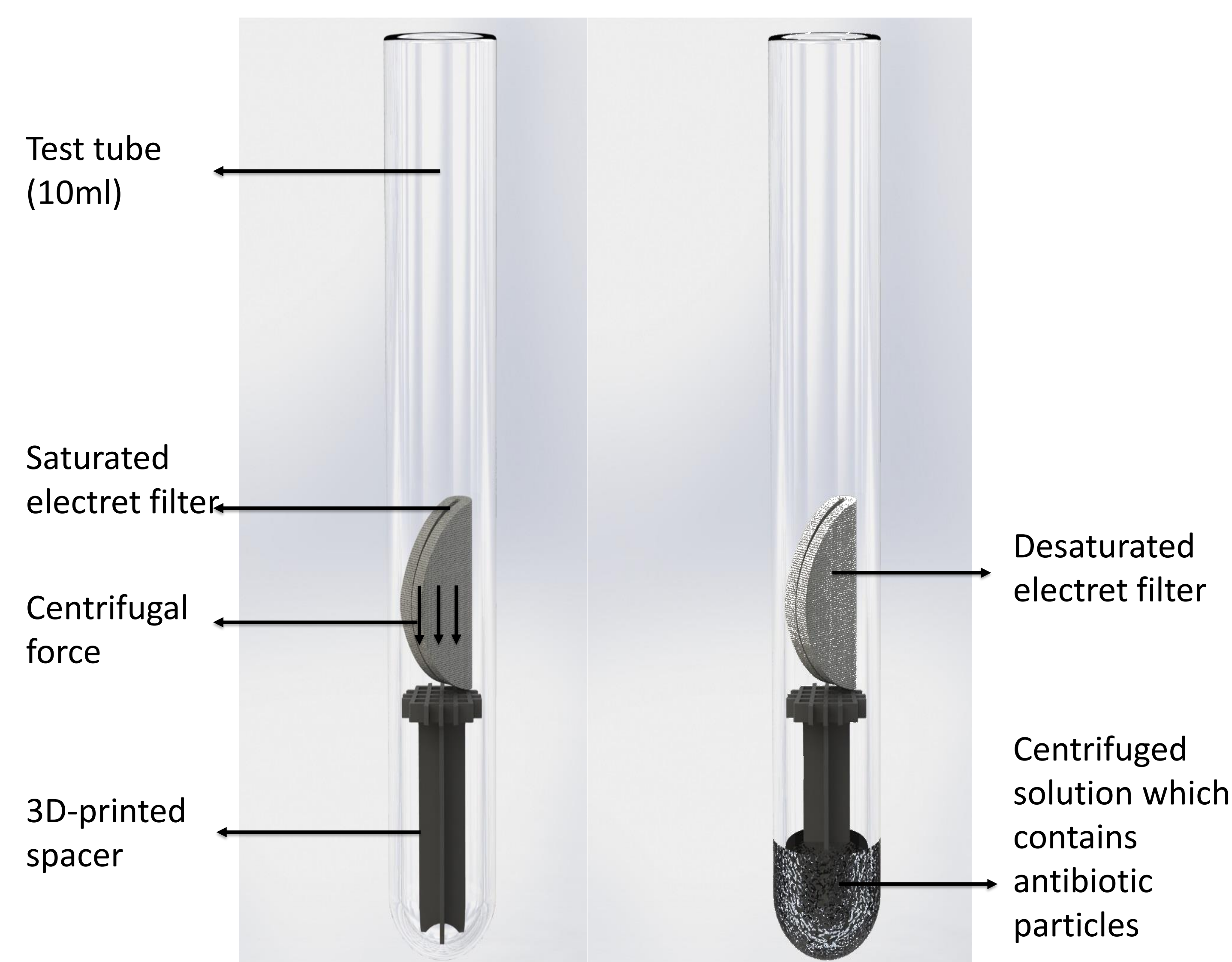


Figure 2. Extraction method for antibiotics in electret filter which is used for exhaled breath sampling.

### Discussion

This pilot trial confirmed that it is possible to use the ExaBreath®-device in critically ill patients, although there were some practical difficulties in exhaling in a coordinated way in 4 out of 11 patients.

Further research is necessary to evaluate the potential use of the ExaBreath®-device in the treatment of infections in the ICU. Sampling patients on mechanically ventilated patients could bypass the difficulties in exhaling in a non-standardized way.

#### References

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2. Beck O, Stephanson N, Sandqvist S et al. Detection of drugs of abuse in exhaled breath using a device for rapid collection: comparison with plasma, urine and self-reporting in 47 drug users. *J Breath Res* 2013; 7(2):026006.
3. Coucke L, Massarini E, Ostijn Z et al. Δ9-Tetrahydrocannabinol concentrations in exhaled breath and physiological effects following cannabis intake – A pilot study using illicit cannabis. *Clin Biochem* 2016; Jun 8, e-pub ahead of print